REMARKS

In view of the above amendments and the following remarks, reconsideration of the outstanding office action is respectfully requested.

The April 29, 2004, telephonic interview between Examiner Hutson and applicants' undersigned attorney is gratefully acknowledged. The substance of that interview is summarized below.

The objection to the specification is respectfully traversed in view of the above amendments.

The rejection of claim 25 under 35 U.S.C. § 112 (2nd para.) is respectfully traversed in view of the above amendments.

The rejection of claims 25, 26, and 29 under 35 U.S.C. § 112 (1st para.) is respectfully traversed in view of the above amendments.

The rejection of claims 25, 26, and 29 under 35 U.S.C. § 102 or 35 U.S.C. § 103 as anticipated by or for obviousness over U.S. Patent No. 6,361,996 to Rao et. al., ("'996 Patent") is respectfully traversed.

The '996 Patent has been fully discussed in previous responses to office actions. Accompanying this amendment is the Declaration of Mahendra S. Rao, M.D., Ph.D. under 37 C.F.R. § 1.132 ("Rao Declaration"). The declarant is the same Dr. Rao who is the co-inventor of the '996 Patent. His declaration is presented to demonstrate why the subject matter of the '996 Patent is very different from that of the present patent application (Rao Declaration ¶ 5).

The '996 Patent discloses multipotential neuroepithelial stem cells and lineage-restricted astrocyte/oligodendrocyte precursor cells (Rao Declaration ¶ 6). The astrocyte/oligodendrocyte precursor cells are derived from neuroepithelial stem cells, are capable of self-renewal, and can differentiate into astrocytes and oligodendrocytes but not neurons (Id.). The '996 Patent characterizes these cells as "multipotential intermediate precursor cells restricted to glial lineages" (emphasis added)(column 23, lines 1-5) (Id.). Similarly, Rao, et. al., "Glial-Restricted Precursors are Derived From Multipotential Neuroepithelial Stem Cells," *Devel. Biol.* 188: 48-63 (1997) clearly demonstrates that such A2B5+/NCAM cells are capable of generating both astrocytes and oligodendrocytes and do not appear committed to the oligodendrocyte lineage (Id.). The '996 Patent's astrocyte/oligodendrocyte precursor cells are in a less differentiated state than the oligodendrocyte-specified progenitor cells of claims 25 and 29 of the present patent

application (Id.). Support for the "oligodendrocyte-specified progenitor" limitation is found on page 14, line 25 of the present application. Therefore, the '996 Patent's astrocyte/oligodendrocyte precursor cells are very different from the cells set forth in claims 25 and 29 of the present application (Id.). This statement by the first-named inventor of the '996 Patent is strong evidence that the enriched or purified preparation of cells in these claims is clearly distinguishable from the astrocyte/oligodendrocyte precursors of the '996 Patent. Accordingly, the rejection of claims 25 and 29 based on the '996 Patent should be withdrawn.

The mitotic oligodendrocyte progenitor cells from an adult human of claim 26 are also distinguishable from the astrocyte/oligodendrocyte precursor cells of the '996 Patent. Differences in the method, time of isolation, and propagation in the '996 Patent and the enriched or purified preparation of cells in claim 26 should also be noted. These cells of the present application were derived from the adult brain using a promoter reporter based strategy where the CNP2 promoter directed expression of green fluorescent protein (Id.). On the other hand, the astrocyte/oligodendrocyte precursor cells of the '996 Patent were derived from fetal and neonatal tissue using cell surface antigen expression and fluorescence-based antibody capture (Id.). No strategy of using CNP2 (a cyctoplasmic marker) expression, a CNP2 promoter, or a related promoter reporter strategy is described in the '996 Patent (Id.).

The '996 Patent is directed to the enrichment of glial progenitor cells from newborn rat brain (Rao Declaration ¶ 8). Newborns have an abundant population of still-developing oligodendrocyte progenitor cells that may constitute a significant fraction of all of the cells in neonatal brain tissue (Id.). Yakovlev, et. al., "A Stochastic Model of Brain Cell Differentiation in Tissue Culture," *J Math Biol.*, 37(1):49-60 (1998); Bogler et. al., "Measurement of Time in Oligodendrocyte-type-2 Astrocyte (O-2A) Progenitors is a Cellular Process Distinct from Differentiation or Division," *Dev Biol.*, 162(2):525-38 (1994); and Raff et. al., "Platelet-derived Growth Factor From Astrocytes Drives the Clock That Times Oligodendrocyte Development in Culture." *Nature* 333(6173):562-65 (1988) describe cell cycle changes as glial progenitor cells mature (Id.). They showed that adult cells differ in their cell cycle time and the number of divisions before they will become postmitotic (Id.). The present patent application discloses this for adult human-derived cells (Id.). In addition, adult-derived human oligodendrocyte progenitor cells differentiate as oligodendrocytes and produce myelin much more quickly than do fetal or neonatal oligodendrocyte progenitor cells (Id.). As recently reported in Nunes et al., "Identification and Isolation of Multipotent Neural

Progenitor Cells from the Subcortical White Matter of the Adult Human Brain," *Nature Medicine* 9:239-247 (2003) and Windrem et al., "Fetal and Adult Human Oligodendrocyte Progenitor Cell Isolates Myelinate the Congenitally Dysmyelinated Brain," *Nature Medicine* 10:93-97 (2004), adult-derived oligodendrocyte progenitor cells not only myelinate much more rapidly than do fetal oligodendrocyte progenitors, but they do so more efficiently, with a higher proportion exhibiting effective myelin production, and myelinating a greater number of neuronal axons per donor cell than their fetal-derived counterparts (Id.). Adult cells are thus fundamentally more biased towards generating oligodendrocytes, towards maturing to express myelin proteins, and towards myelinating host axons (Id.). Moreover, adult cells execute all of these functions, and achieve each of these cellular milestones, much more quickly than fetal cells (Id.). As a result, they lend themselves to a very different set of potential clinical targets than fetal or neonatal-derived progenitors, as recently reported in Roy et al., "Progenitor Cells of the Adult Human Subcortical White Matter In: *Myelin Biology and Disorders*, vol. 1. R. Lazzarini, ed. Elsevier:Amsterdam, pp. 259-287 (2004) (Id.). Adult oligodendrocyte progenitor cells are thus fundamentally different from fetal or neonatal-derived progenitors (Id.). This is yet another reason why the '996 Patent's rat fetal astrocyte/oligodendrocyte precursor cells are very different from the adult oligodendrocyte progenitor cells in claim 26 of the present application (Id.).

For all of these reasons the rejection of claims 25, 26, and 29, based on the '996 Patent, should be withdrawn.

In view of all of the foregoing, applicants submit that this case is in condition for allowance and such allowance is earnestly solicited.

Respectfully submitted,

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